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68/822,186	03/20/97	RUEGER	D CRP-137

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EXAMINER

ROMEO, D

ART UNIT

PAPER NUMBER

1646

DATE MAILED:

08/04/98

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

Office Action Summary	Application No. 08/822,186	Applicant(s) Rueger et al.
	Examiner <i>David Romeo</i> David Romeo	Group Art Unit 1646

☒ Responsive to communication(s) filed on May 11, 1998

☒ This action is **FINAL**.

☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

A shortened statutory period for response to this action is set to expire 3 month(s), or thirty days, whichever is longer, from the mailing date of this communication. Failure to respond within the period for response will cause the application to become abandoned. (35 U.S.C. § 133). Extensions of time may be obtained under the provisions of 37 CFR 1.136(a).

Disposition of Claims

☒ Claim(s) 1-33, 35, and 36 is/are pending in the application.

Of the above, claim(s) _____ is/are withdrawn from consideration.

☐ Claim(s) _____ is/are allowed.

☒ Claim(s) 1-33, 35, and 36 is/are rejected.

☐ Claim(s) _____ is/are objected to.

☐ Claims _____ are subject to restriction or election requirement.

Application Papers

☐ See the attached Notice of Draftsperson's Patent Drawing Review, PTO-948.

☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

☐ The proposed drawing correction, filed on _____ is ☐ approved ☐ disapproved.

☐ The specification is objected to by the Examiner.

☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

☐ All ☐ Some* ☐ None of the CERTIFIED copies of the priority documents have been

☐ received.

☐ received in Application No. (Series Code/Serial Number) _____.

☐ received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

*Certified copies not received: _____

☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

☒ Notice of References Cited, PTO-892

☐ Information Disclosure Statement(s), PTO-1449, Paper No(s). _____

☐ Interview Summary, PTO-413

☐ Notice of Draftsperson's Patent Drawing Review, PTO-948

☐ Notice of Informal Patent Application, PTO-152

☒ Attachment #1 to Paper No. 9

--- SEE OFFICE ACTION ON THE FOLLOWING PAGES ---

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DETAILED ACTION

1. The Group and/or Art Unit location of your application in the PTO has changed. To aid in correlating any papers for this application, all further correspondence regarding this application should be directed to Group Art Unit 1646.
- 5 2. The amendment filed 11 May 1998 (Paper No. 8) has been entered in full.
3. Claims 1-33, 35 and 36 are pending and are being examined.
4. The objection to claim 2 is withdrawn in view of Applicants' amendment.
5. The objection to claim 18 is withdrawn in view of Applicants' amendment.

Response to Arguments

- 10 6. The rejection of claims 2-4 under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a device comprising an osteogenic protein wherein said osteogenic protein is selected from the specifically recited osteogenic proteins, or wherein said osteogenic protein comprises an amino acid sequence having at least 70% homology with the C-terminal 102-106 amino acids, including the conserved seven cysteine domain, of human OP-1

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and induces local bone and or cartilage formation, does not reasonably provide enablement for a device comprising an osteogenic protein wherein said osteogenic protein is an amino acid sequence variant of the specifically recited osteogenic proteins or wherein said osteogenic protein comprises an amino acid sequence having at least 70% homology with the C-terminal 102-106 amino acids, including the conserved seven cysteine domain, of human OP-1 without regard to the functional activity of the osteogenic protein, is maintained.

Applicants argue that the instant specification complies with the legal standard of 35 U.S.C. § 112, first paragraph. Applicant's arguments have been fully considered but they are not persuasive. Although the specification provides for a functional activity of an osteogenic protein, the claims do not provide a functional activity for "conservative amino acid sequence variants" of or proteins having 70% homology to the osteogenic proteins. Although, the claims are interpreted in light of the specification, limitations from the specification are not read into the claims. Although the claims have been limited to "conservative amino acid sequence variants" the claims encompass polypeptides with an unlimited number of conservative amino acid substitutions. Because the effects of mutations are cumulative, it is unlikely that the proteins of the instant invention can tolerate an unlimited number of amino acid substitutions and retain their functional activity. Furthermore, the effects of mutations are unpredictable. See Bowie et al. (UU) page 1306, column 1, full paragraph 1, wherein it is taught that predicting structure, hence function, from primary amino acid sequence data is extremely complex, and it unlikely the

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problem will be solved in the near future. It is likely that there are an large number of inoperable embodiments encompassed by the phrases "conservative amino acid sequence variants" and "70% homology", which the specification has not taught how to use in the claimed device absent undue experimentation.

5 7. The rejection of claims 26-30, 34 under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention, is withdrawn in view of Applicants' amendment.

8. The rejection of claims 1, 7-15, 20-22, 24 under 35 U.S.C. 102(b) as being anticipated by Amman et al. (A), is maintained. Applicants argue that Amman et al. do not disclose an
10 osteogenic protein, that TGF- β does not fall within Applicants' definition of an osteogenic protein and that the specification at page 22, lines 3-7 makes it clear that TGF- β is not an osteogenic protein. Applicant's arguments have been fully considered but they are not persuasive.

While applicant may be his or her own lexicographer, a term in a claim may not be given a meaning repugnant to the usual meaning of that term. See *In re Hill*, 161 F.2d 367, 73
15 USPQ 482 (CCPA 1947). The term "osteogenic" in the claims is used by the claims to mean "endochondral bone formation", while the accepted meaning is "bone formation". See Attachment 1. Applicants are defining the term more narrowly than it would be defined by the

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skilled artisan. In accordance with the accepted meaning of the term "osteogenic", Amman et al. clearly identify TGF- β as an osteogenic protein (column 5, full paragraph 4). The fact that the specification identifies TGF- β as a growth factor (page 22, lines 3-7) does not exclude TGF- β as an osteogenic protein, as evidenced by Amman et al. The claims do not distinguish the osteogenic
5 protein used in the claimed device from the TGF- β used by Amman et al., and Amman et al. anticipate the claimed invention.

9. The rejection of claims 1-4, 7-15 under 35 U.S.C. 102(b) as being anticipated by O'Leary (C), is withdrawn in view of Applicants' amendment.

10. The rejection of claims 23 and 24 under 35 U.S.C. 102(b) as being anticipated by
10 Lindstrom et al. (B), is maintained. Applicants' argue TGF- β is not an osteogenic protein. Applicant's arguments have been fully considered but they are not persuasive, as discussed above, and that discussion is incorporated herein by reference.

11. The rejection of claims 1 and 6 under 35 U.S.C. 103(a) as being unpatentable over
O'Leary et al. (C) as applied to claim 1 above, and further in view of Ogawa et al. (U) is
15 withdrawn in view of Applicants' amendment.

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12. The rejection of claims 1 and 9 under 35 U.S.C. 103(a) as being unpatentable over Amman et al. (A) in view of LeGeros et al. (CS, cited by Applicants) is maintained. Applicants' argue TGF- β is not an osteogenic protein. Applicant's arguments have been fully considered but they are not persuasive, as discussed above, and that discussion is incorporated herein by
5 reference. The combined references teach all of the elements of claim 9.

13. The rejection of claims 1, 20-22, 32 and 33 under 35 U.S.C. 103(a) as being unpatentable over Amman et al. (A) is maintained. The rejection of record is applied to claims 35 and 36. Applicants' argue TGF- β is not an osteogenic protein. Applicant's arguments have been fully considered but they are not persuasive, as discussed above, and that discussion is incorporated
10 herein by reference.

14. The rejection of claims 23, 24 and 26-30 under 35 U.S.C. 103(a) as being unpatentable over Lindstrom et al. (B) is maintained. Applicants' argue TGF- β is not an osteogenic protein. Applicant's arguments have been fully considered but they are not persuasive, as discussed above, and that discussion is incorporated herein by reference.

15. The rejection of claims 1, 5, 17-19 and 26-31 under 35 U.S.C. 103(a) as being unpatentable over Cook et al. (CD, cited by Applicants) in view of O'Leary et al. (C) is

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maintained. Applicants' argue that O'Leary does not teach the use of collagen without demineralized bone and therefore O'Leary et al. teach away from the claimed invention.

Applicant's arguments have been fully considered but they are not persuasive. In contrast to the fact situation of In re Gurely, O'Leary et al. do not teach that collagen is inferior to bone powder.

5 Furthermore, O'Leary et al. do not suggest that collagen is unlikely to be productive or useful in Applicants' device. Like the facts situation of In re Gurely, in which the court found that Gurley's "teaching away" argument insufficient, the use of collagen was known and collagen had been used by Cook et al. for Applicants' purpose, i.e. bone formation, and Applicants have not distinguished their composition from the composition taught by Cook et al. in view of O'Leary. Cook et al.
10 teach a composition comprising collagen and BMP for bone formation. O'Leary et al. teach a composition for bone formation comprising carboxymethylcellulose (CMC) and O'Leary et al. also teach that carboxymethylcellulose significantly improves the ability of the composition to keep the bone powder in suspension and makes the application of a homogeneous composition easier. One of ordinary skill in the art would be motivated to modify the composition of Cook et
15 al. by including CMC, as taught by O'Leary et al., in order to improve the ability of the composition to keep the collagen in suspension and make application of a homogeneous composition easier. The invention remains prima facie obvious over the prior art.

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16. The rejection of claims 1, 15-19 and 25 under 35 U.S.C. 103(a) as being unpatentable over Cook et al. (CD, cited by Applicants) in view of O'Leary et al. (C). as applied to claims 1, 17-19 above, and further in view of Kuberasampath et al. (AE, cited by Applicants) is maintained. Applicants' argue that O'Leary does not teach the use of collagen without demineralized bone and therefore O'Leary et al. teach away from the claimed invention. Applicant's arguments have been fully considered but they are not persuasive. Applicants arguments of "teaching away" are insufficient to establish non-obviousness, as discussed above, and that discussion is incorporated herein by reference. The invention remains prima facie obvious over the prior art.

Claim Rejections - 35 USC § 102

17. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless --

(e) the invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application by another who has fulfilled the requirements of paragraphs (1), (2), and (4) of section 371(c) of this title before the invention thereof by the applicant for patent.

18. Claims 1-4 are rejected under 35 U.S.C. 102(e) as being anticipated by Kuberasampath et al. (AA). Kuberasampath et al. disclose a device comprising an osteogenic protein (Abstract),

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wherein the osteogenic protein is OP-1 (column 3, full paragraph 2), a matrix derived from a non-synthetic, non-polymeric material other than demineralized bone, i.e. collagen and glycosaminoglycan (column 2, full paragraph 3; column 5, full paragraphs 1-2), and a binding agent, i.e. methyl cellulose (column 3, full paragraph 1).

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Claim Rejections - 35 USC § 103

19. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

20. Claims 1 and 6 are rejected under 35 U.S.C. 103(a) as being unpatentable over Kuberasampath et al. (UU) as applied to claim 1 above, and further in view of Ogawa et al. (U).

10 Kuberasampath et al. teach the device of claim 1, as discussed above. Kuberasampath et al. do not teach said device comprising at least two different osteogenic proteins. Ogawa et al. teach that TGF- β and BMP synergize in promoting the formation of endochondral bone *in vivo* (page 14233, paragraph bridging columns 1-2). TGF- β is an osteogenic protein. Op-1 is a BMP. Ogawa et al. do not teach the device of claim 1 comprising TGF- β and BMP. However, it would

15 have been obvious to one of ordinary skill in the art at the time of Applicants' invention to make the claimed device, as taught by Kuberasampath et al., and to modify that teaching by including two different osteogenic proteins, such as TGF- β and BMP, as taught by Ogawa et al., with a

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reasonable expectation of success. One of ordinary skill in the art would be motivated to combine these teachings in order to achieve the synergistic effect of two different osteogenic proteins and induce more bone growth. The invention is prima facie obvious over the prior art.

Conclusion

5 21. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

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Any inquiry concerning this communication or earlier communications from the examiner should be directed to David S. Romeo whose telephone number is (703) 305-4050. The examiner can normally be reached on Monday through Friday from 8:00 a.m. to 4:30 p.m.

5 If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Lila Feisee, can be reached on (703) 308-2731.

Official papers filed by fax should be directed to (703) 308-4242.

Faxed draft or informal communications should be directed to the Examiner at (703) 308-0294.

10 Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (703) 308-0196.

Elizabeth C. Kemmerer

ELIZABETH KEMMERER
PRIMARY EXAMINER

DSR *qsl*
August 1, 1998